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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File copy	09/535,364	COMB ET AL.	
	Examiner	Art Unit	
	Tomas Friend	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,21,22 and 27-38* is/are pending in the application.

4a) Of the above claim(s) *19,21,22 and 34-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-33* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Action

Change of Art Unit Designation

Please note: The Art Unit location of this application in the PTO has changed from Art Unit 1627 to Art Unit 1639. To aid in matching papers to this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Change of Examiner

The examiner of this application has changed from P. Ponnaluri to Tomas Friend.

Status of the Application

Receipt is acknowledged of a response to a communication from the examiner on 13 November 2002 (Paper No. 17).

Status of the Claims

Claims 19, 21, 22, and 27-38 are pending in the present application. Claims 19, 21, 22, and 34-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

Information Disclosure Statement

The Information Disclosure Statement filed 07 June 2000 (Paper No. 3) includes over 50 references, which have been considered only to the extent possible, given the time available to the examiner to examine the application.

Response to Restriction and Election of Species with Traverse

Applicants' election with traverse of Group V, claims 27-29 (in part), 30, 31, 32 (in part), and 33 in Paper No. 13 is acknowledged. Applicant's election with traverse of phosphorylated Akt consensus motifs as species of kinase consensus motif in Paper Nos. 13 and 17 is acknowledged. The traversal is on the ground(s) that [1] Groups V-VIII represent preferred species or subsets of a single novel class of antibodies and [2] the search of Groups V-VIII would not be burdensome because the Groups are in the same class and subclass and different fields of search are not required. This is not found persuasive because the different groups are drawn to different groups of antibodies (each encompassing numerous species) that bind to structurally distinct antigens. Consequently, the search terms used for each of Groups V-VIII would require different combinations of search terms. Applicants did not traverse the restriction between Group V and Groups I – IV.

The requirement is still deemed proper and is therefore made FINAL.

Objections to the Specification and Claims

1. Claim 32 is objected to because of the following informalities: "*with*" in the last line of the claim should be "*within.*" Appropriate correction is required.

2. The specification is objected to over the length and content of the abstract. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

3. On page 34 of the specification, last paragraph, it appears that "*in –1 position by proline*" should be "*in +1 position by proline.*"

Claims Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 27-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (written description).

The antibodies encompassed by the present claims include monoclonal and polyclonal antibodies from any species that bind to any motif including a phosphorylated, acetylated, or methylated amino acid found in any cell signaling protein or any kinase substrate motif or protein-protein binding motif including at least one phosphorylated amino acid. This includes thousands of motifs comprising large numbers of different sequences that serve as substrates for one or more kinases as well as many thousands of different species including, for example, different bacteria, fungi, mammals, and reptiles. Additionally, the claims encompass antibodies that bind to modified motifs that comprise multiple modifications in addition to phosphorylation, acetylation, and methylation, including combinations of these as well as modification with nucleosides, for example. The predictability that antibodies can be raised against any modified sequence was low because not all modified peptides or amino acids are equally antigenic. The

development of anti-phosphoserine and anti-phosphothreonine antibodies, for example, lagged behind the development of phosphotyrosine antibodies.

The present specification provides examples of antibodies that bind to the following "*motifs:*" phosphothreonine; RXS*XP; RSXS*XP; PXT*/S*PXR; acetylated lysine; RXRXXT*; RRXT*; and [F/Y][T*/S*] or [S*/T*]F.

The specification does not indicate that applicants are in possession of any other antibodies encompassed by the rejected claims nor are these examples representative of the antibodies encompassed by present claims, which would bind to any one of many thousands of different modified sequences. Antibodies that bind to any one of the other large number of different motif sequences and to multiply modified motif sequences such as those with more than one phosphate or combinations of phosphorylated and acetylated amino acids are not represented.

Claims Rejections – 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 27-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 27, it is not clear if "*cell signaling proteins within a genome*" is intended to have the same meaning as "*cell signaling proteins expressed from genes within a genome*" or if some other meaning is intended.

B. In claims 27, 28, and 32, the meaning of "*peptides or proteins within said genome*" is not clear because a genome is comprised of nucleic acid and not peptides or proteins.

Claims Rejections – 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 27-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Tani et al. U.S. Patent 6,001,580 December 1999. Miceli et al. J. Immunological Methods 167 :279-287 (1994) is cited to document the generally motif-specific, context independent nature of antibody-antigen binding.

The claimed invention is drawn to a motif-specific, context independent antibody that binds a MAP kinase consensus motif comprising at least one phosphorylated amino acid. A motif-specific, context independent antibody is defined in the specification as being specific against one or more fixed amino acid residues in the context of variable surrounding peptide or protein sequences.

The '580 patent discloses an anti-MAP kinase antibody capable of specifically binding to activated (i.e. phosphorylated) human and rat MAP kinases ERK1 and ERK2 at the SEQ. I.D. No. 1 epitope (i.e. more than one fixed amino acid residue). The antibody binds to SEQ. I.D. No. 1 of the reference in at least four different proteins (i.e. variable surrounding protein sequences). Column 25, lines 34-35, discloses that MAP kinase is activated (i.e. phosphorylated) by MAP kinase (i.e. SEQ. I.D. No. 1 of the reference comprises a MAP kinase consensus motif). Consequently, SEQ I.D. No. 1 comprises a MAP kinase phosphorylation motif. Both

monoclonal and polyclonal antibodies against activated ERK1 and ERK2 are disclosed. Accordingly, present claims 27-31 are anticipated by the '580 patent.

With respect to present claims 32 and 33 it appears that the antibody disclosed in the '580 reference is indistinguishable from the product by process antibody recited in claim 32. The motif-specific, context independent nature of antibody-antigen binding was known in the art as illustrated by Miceli et al. Miceli et al. disclose that epitope mapping of a monoclonal antibody (M2) raised against the FLAG sequence recognizes numerous peptides. The peptides recognized by the antibody share three fixed amino acid positions (See Figure 4). The peptides recognized by M2, however, may include a wide variety of amino acids at positions surrounding the fixed amino acid positions. The reference discloses that peptide libraries had been used to study cross-reactive peptides that bind to antibodies, indicating that such cross-reactivity was a common occurrence, if not inherent, in the nature of antibody-epitope interactions.

Present claims 32 and 33 are product by process claims. The antibodies disclosed in the '580 patent are presumed to be structurally and functionally indistinguishable from those encompassed by the presently claimed antibodies. The present specification provides no biochemical results demonstrating structural or functional differences between the antibodies of present claim 32 and antibodies disclosed in the prior art.

7. Claims 27-33 are rejected under 35 U.S.C. 102(a) and under 35 U.S.C. 102(e) as being anticipated by Strulovici U.S. Patent No. 5,759,787 June 1998.

The claimed invention is drawn to a motif-specific, context independent antibody that binds a MAP kinase consensus motif selected from the group consisting of MAPK, CDK, PKA, and Akt, comprising at least one phosphorylated amino acid. A motif-specific, context independent antibody is defined in the specification as being specific against one or more fixed amino acid residues in the context of variable surrounding peptide or protein sequences.

The '787 patent discloses a monoclonal antibody, YC10, which recognizes phosphoserine in the context of TS(P)AARR (i.e. the fixed amino acid positions in the context of variable protein sequences which surround them). The recognized sequence is phosphorylated by PKA (i.e. contains a consensus motif for PKA).

The '787 patent also discloses a monoclonal antibody that recognizes phosphorylated epitopes on mitotic proteins and antibodies that recognize phosphorylated tyrosine, serine, or threonine residues (i.e. antibodies specific for broader phosphorylation substrate motifs such as tyrosine kinase or serine-threonine kinase substrates).

With respect to present claims 32 and 33 it appears that the antibody disclosed in the '580 reference is indistinguishable from the product by process antibody recited in claim 32. The motif-specific, context independent nature of antibody-antigen binding was known in the art as illustrated by Miceli et al. Miceli et al. disclose that epitope mapping of a monoclonal antibody (M2) raised against the FLAG sequence recognizes numerous peptides. The peptides recognized by the antibody share three fixed amino acid positions (See Figure 4). The peptides recognized by M2, however, may include a wide variety of amino acids at positions surrounding the fixed amino acid positions. The reference discloses that peptide libraries had been used to study cross-reactive peptides that bind to antibodies, indicating that such cross-reactivity was a common occurrence, if not inherent, in the nature of antibody-epitope interactions.

Present claims 32 and 33 are product by process claims. The antibodies disclosed in the '787 patent are presumed to be structurally and functionally indistinguishable from those encompassed by the presently claimed antibodies. The present specification provides no biochemical results demonstrating structural or functional differences between the antibodies of present claim 32 and antibodies disclosed in the prior art.

Conclusion

8. No claims are allowed.

9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner works on a flexible schedule of four ten-hour days per week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

Tomas Friend, Ph.D.
22 February 2003

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600